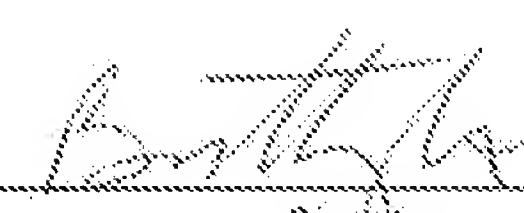


Doc Code: AP.PRE.REQ

PTO/SB/33 (07-09)

Approved for use through 07/31/2012 OMB 0651-0001
U.S. Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional)	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on _____ Signature _____ Typed or printed name _____		Application Number	Filed
		10/550,383	March 29, 2007
		First Named Inventor	
		Michael G. Orchard et al.	
		Art Unit	Examiner
		1625	John Mabry
Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.			
This request is being filed with a notice of appeal. ✓			
The review is requested for the reason(s) stated on the attached sheet(s). ✓ Note: No more than five (5) pages may be provided.			
I am the:			
<input type="checkbox"/> applicant/inventor.		Signature	
<input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/86)		Brittany La	
		Typed or printed name	
<input checked="" type="checkbox"/> attorney or agent of record. Registration number 58,337		973-912-6232	
		Telephone number	
<input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____		March 7, 2011	
		Date	
NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.			
<input checked="" type="checkbox"/> *Total of 1 forms are submitted.			

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by this USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Michael G. Orchard et al.	Examiner:	John Mabry
Serial No.:	10/560,383	Group Art Unit:	1625
Filed:	March 29, 2007	Docket No.:	AC-50-US
Title:	2-HYDROXYMETHYL-3,4,5- TRIHYDROXY-1-(4-PENTYLOXYBENZYL) PIPERIDINE AS GLYCOSYLCERAMIDE SYNTHASE (GCS) INHIBITORS	Confirmation No.:	9092

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir/Madam:

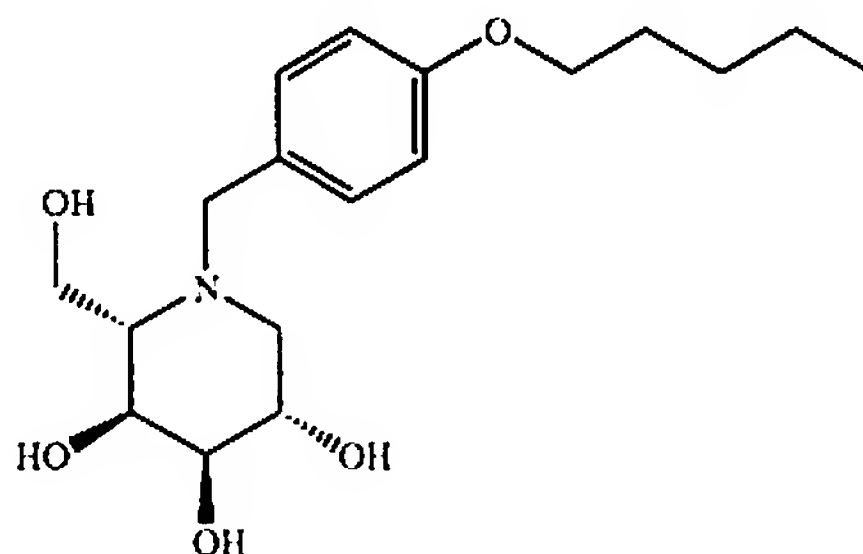
In response to the Final Office Action dated December 7, 2010 and the Advisory Action dated February 3, 2011, Applicants respectfully request for a Pre-Appeal Brief Review of this case for reversal of the Examiner's rejections of the claims based on clear errors. In support of the request, Applicants hereby submit the following and respectfully request for consideration:

Notice of Appeal — attached hereto;
PTO/SB/33 — attached hereto;
REMARKS — pages 2-5;
Exhibit A — Listing of the Claims – attached hereto;
Exhibit B – U.S. Appl. No. 10/522,207 – attached hereto

REMARKS

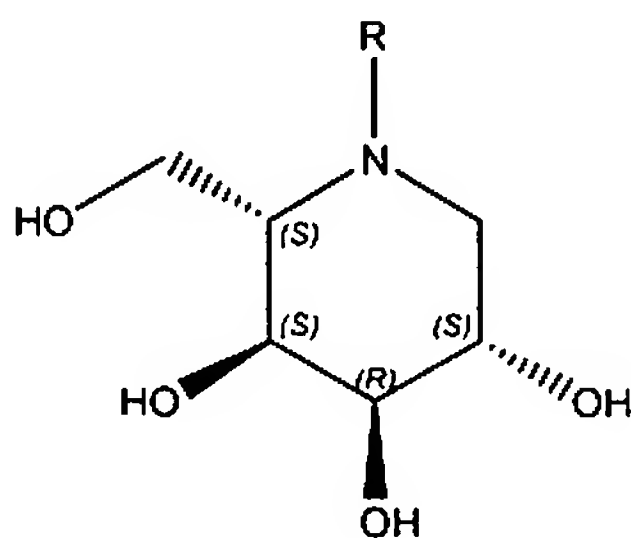
Claims 1, 3 and 20 are pending. Claims 2 and 5-19 were cancelled. Claims 4 and 21-35 were withdrawn. Claims 1 and 3 (and 20)¹ have been provisionally rejected for being unpatentable over claims 1-10 and 13 of co-pending application number 10/522,207 (the '207 application) on the ground of non-statutory obviousness-type double patenting.

Claim 1 of the current application is directed to the compound 3,4,5-piperidinetriol, 2-(hydroxymethyl)-1-[(4-(pentyloxy)phenyl)methyl]-, (2S,3S,4R,5S):



in free or a pharmaceutically acceptable salt form and claim 3 is directed to a composition comprising the same.

Claim 1 of the '207 application is directed to a compound of formula (I) in free or pharmaceutically acceptable salt form:



(I)

“wherein

R is -C₁₋₃ alkylAr¹ where Ar¹ is phenyl;

wherein phenyl is substituted by one or more substituents selected from CN, CON(R¹)₂, SO_nR², SO₂N(R¹)₂, N(R⁵)₂, N(R¹)COR², N(R¹)SO_nR², C₀₋₆ alkylAr², C₂₋₆ alkenylAr² and C₃₋₆ alkynylAr²...

¹ The Examiner noted in the Final Office Action Summary dated 12/7/2011 that claim 20 is allowable. The Advisory Action dated February 10, 2011 noted however, that claim 20 is rejected. Applicants hereby seek clarification as to the status of this claim.

and the Ar¹ phenyl is optionally substituted by one or more additional substituents selected from F, Cl, Br, CF₃, OCF₃, OR³ and C₁₋₆ alkyl; . . .
R³ is H, or C₁₋₆ alkyl;”.

The Examiner argued that claims 1 and 3 of the current application are unpatentable in view of claims 1-10 and 13 of the ‘207 application because “the species of the instant application is encompassed by the genus as claimed in US ‘207”. *Office Action* 12/7/2010, page 5. The Examiner therefore rejected the claims on the ground of obviousness-double patenting.

Applicants respectfully disagree. Applicants first take this opportunity to clarify the following: while it is true that the R substituent of the compound of Formula I of the ‘207 Application may be –C₁₋₃alkyl Ar¹ wherein the Ar¹ phenyl may optionally be substituted with one or more additional substituents selected from, among others, OR³ wherein R³ may be H or C₁₋₆alkyl, Applicants correct the statement made in the response filed February 7, 2011 and disagrees with the Examiner that the claims of the current application and the claims of the ‘207 application have patentably indistinct genus-species relationship. Generic claim 1 of the ‘207 application requires that the Ar¹ phenyl of the –C₁₋₃ alkylAr¹ be substituted with one or more substituents selected from “CN, CON(R¹)₂, SO_nR², SO₂N(R¹)₂, N(R⁵)₂, N(R¹)COR², N(R¹)SO_nR², C₀₋₆ alkylAr², C₂₋₆ alkenylAr² and C₃₋₆ alkynylAr²...” and provides that Ar¹ phenyl may optionally be substituted with one or more additional substituents selected from, among others, OR³ wherein R³ may be H or C₁₋₆alkyl. (Emphasis added). As such, the Ar¹ phenyl is only additionally substituted with, among others, OR³ if Ar¹ is first substituted with one or more substituents selected from “CN, CON(R¹)₂, SO_nR², SO₂N(R¹)₂, N(R⁵)₂, N(R¹)COR², N(R¹)SO_nR², C₀₋₆ alkylAr², C₂₋₆ alkenylAr² and C₃₋₆ alkynylAr²...”. In other words, OR³ substituent is a selection when Ar¹ phenyl is di-, tri-substituted, etc. In contrast, the compound of the currently claimed invention is specifically mono-substituted at the benzyl substituent with a pentyloxy group. Consequently, the compound of the current invention is patentably distinct from those claimed in the ‘207 application and the Examiner has erroneously interpreted the claims in the ‘207 application.

Even if the claims of the current invention have a genus-species relationship with the claims of the ‘207 application, MPEP 804 explicitly warned that: “[d]omination [i.e., when one patent or application has a broad or generic claim which fully encompasses or reads on an

invention defined in a narrower or more specific claim in another patent or application] by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection.” MPEP 804, citing *In re Kaplan*, 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964). If not based on anticipation, the obviousness-type double patenting determination should parallel the guidelines for a 35 U.S.C. 103(a) rejection. MPEP 804. In this regard, the Federal Circuit has held that a disclosure of a generic formula does not by itself render obvious a species of that genus, *See In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994) (“The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.”)(Citation omitted). Extending the analysis of *Baird*, a claim covering a genus does not by itself render a claim covering the species patentably indistinct and unpatentable.

In analyzing obviousness under § 103(a), the Federal Circuit clearly stated in *Eisai Co. LTD v. Dr. Reddy's Laboratories, LTD.*, 533 F.3d 1353 (Fed. Cir. 2008) that “a prima facie case of obviousness for a chemical compound [] begins with the reasoned identification of a lead compound.” *Id.* at 1359. Also in *Takeda Chemical Industries, LTD v. Alpharm PTY., LTD*, 492 F.3d 1350 (Fed. Cir. 2007), the Court stated that “[i]n addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of ‘adequate support in the prior art’ for the change in structure.” *Id.* at 1356. In the recent case *Daiichi Sankyo Co., LTD. v. Matrix Lab. LTD.*, 2010 WL 3504759 (Fed. Cir. 2010), the Court again reiterated that “proving a reason to select a compound as a lead compound depends on more than just structural similarity, but also knowledge in the art of the functional properties and limitations of the prior art compounds. [] Potent and promising activity in the prior art trumps mere structural relationships.” *Id.* at *5 (emphasis added). In particular, the Court explained: “it is the possession of promising useful properties in a lead compound that motivates a chemist to make structurally similar compounds”, warning that “attribution of a compound as a lead compound after the fact must avoid hindsight bias”. *Id.*

Here, the Examiner committed clear errors in interpreting the claims of the ‘207 application to be patentably indistinct from the claims of the current invention. The Examiner further committed clear errors in ignoring the explicit warning in MPEP Section 804 and

rejecting the claims of the current invention based solely on the erroneous ground that claims of the co-pending '207 application dominates the claims of the current application. In doing the obviousness-type double patenting analysis, the Examiner also failed to provide any rationale whatsoever as to why the claims of the current invention are obvious and patentably indistinct from those of the '207 application. Specifically, the Examiner failed to follow the lead-compound test by failing to identify a reason for plucking the --OR³ substituent from the group of substituents listed in claim 1 of the '207 application and ignoring that the Ar¹ phenyl must also be substituted with other specific substituents so as to arrive at the current invention. None of the specific compounds claimed in claim 11 are actual exemplification of a compound wherein Ar¹ phenyl is additionally substituted with OR³. Nothing in the claims (or the specification) of the '207 application points a skilled artisan to select the currently claimed compound as the compound of choice to pursue out of a large number of possibilities. The Examiner can only identify the currently claimed compound as the compound of choice based on improper hindsight knowledge of the current invention.

Wherein the Examiner has misinterpreted the claims in the '207 application, failed to express a well-reasoned analysis and used hindsight knowledge of the current invention to select from the possibilities set out in claims of the '207 application, the specific substituents so as to arrive at the current invention, the Examiner has committed clear errors in the obviousness-type double patenting analysis. Reconsideration and reversal of the rejections of claims 1 and 3 (and 20) are earnestly requested.

Respectfully submitted,

Dated: March 7, 2011

By 
Brittany La
Reg. No. 58,337
HOXIE & ASSOCIATES L.L.C.
75 Main Street, Suite 301
Millburn, NJ 07041
(973) 912-5232